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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/171,081	12/14/98	KRANJC	S 22681-0002

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EXAMINER

FRATS, F

ART UNIT	PAPER NUMBER
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1651

DATE MAILED:

03/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/171,081

Applicant(s)

KRANJC ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-35 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 15-35 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

1. The preliminary amendment filed December 14, 1998, has been received and entered.
2. Claims 1-14 have been cancelled.
3. Claims 15-34 have been added as per applicant's instructions.

However, the numbering of claims in the amendment is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are cancelled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

The preliminary amendment of December 14, 1998, did not cancel originally filed claim 15. Because claim 15 is still pending, the subsequently filed claims should have been renumbered beginning at claim 16.

Thus, misnumbered claims 15-34 have been renumbered as 16-35.

4. Claims 15-35 are pending and are examined on the merits.

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Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claim 15 depends from cancelled claim 14. Therefore it is not clear what subject matter is encompassed by the claim. Claim 15 will be construed as if it depended directly from current claim number 16.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 15-27 and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165).

Cole discloses processes of making clavulanic acid wherein the claimed microorganism, *Streptomyces clavuligerus*, is cultivated in a fermentation medium. Note specifically the potassium dihydrogen phosphate concentration of 0.1% in the fermentation disclosed in Example 13 at column 23. Note further that about 55% of the dipotassium hydrogen phosphate in the fermentation medium in Example 9, at column 21, is "assimilable" phosphorus, i.e. phosphate, and that therefore the medium in Example 9 contains about 1.10 grams of assimilable phosphorus per liter of medium which is about 0.11% assimilable phosphorus, well within the claimed range concentration. Therefore, in at least Examples 9 and 13, the starting phosphorus concentration is below the claimed amount. Moreover, no phosphorus is added during the fermentation, and the fermentations last for 3-5 days. Thus, the processes disclosed in Examples 9 and 13

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necessarily meet the limitation requiring the phosphorus concentration to decrease as the fermentation proceeds.

Cole differs from the claims in that Cole does not disclose any specific examples wherein both the claimed nitrogen and phosphorus amounts are used in a fermentation process. However, Cole clearly discloses that 0.1 to 10% nitrogen may be used in the fermentative production of clavulanic acid. See column 10, lines 29-31. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have been motivated by Cole's disclosure of the suitability of up to 10% nitrogen to have varied the nitrogen amounts used in the Examples, and thereby employed nitrogen in the claimed amount of greater than 5%. Thus, absent some disclosure of an unexpected result inhering from the process as claimed, the claimed amount of nitrogen must be considered obvious over the cited reference.

Further still, official notice is taken of the fact that fed batch and continuous processes as recited in claim 33 were well known at the time of applicant's invention, as were the advantages of those techniques. Thus, the artisan of ordinary skill clearly would have been motivated to have used the claimed techniques for their known advantages, the selection of a specific fermentation technique being an obvious matter of selecting from among known equivalent fermentation techniques.

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Further still, the selection and amount of medium as recited in claims 34 and 35, including scaling up, clearly would have been a routine matter of optimization on the part of the artisan of ordinary skill, fermentation quantity clearly being a result-effective parameter routinely optimized by the artisan of ordinary skill at the time of applicant's invention. Therefore, absent some demonstration of an unexpected result inhering from these parameters, the claims must be considered obvious.

10. Claims 15-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165) in view of Lawrence et al (British Patent 1 571 888).

As discussed above, Cole renders obvious the process recited in claims 15-27 and 30-35. Cole differs from the claims 28 and 29 in not disclosing the use of ammonium sulfate as the nitrogen source. However, Lawrence clearly discloses that inorganic salts including ammonium and sulfate ions can be used as nutrients in culture media used to produce clavulanic acid from *Streptomyces clavuligerus* by fermentation. See page 2, lines 34-37. Thus, the artisan of ordinary skill, recognizing from Lawrence the suitability of salts including ammonium and sulfate ions as nutrients in culture media used to produce

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clavulanic acid from *Streptomyces clavuligerus* by fermentation, clearly would have been motivated to have used ammonium sulfate in the fermentation processes of Cole, reasonably expecting from Lawrence that successful production of clavulanic acid would result.

11. Claims 15-35 rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165) in view of Lawrence et al (British Patent 1 571 888) as applied to claims 15-35 above, and further in view of Puentes et al (EP 0 182 522 A1).

As discussed above, Cole obviates claims 15-35 when taken in view of Lawrence. With the exception of *Streptomyces clavuligerus*, neither of those references discloses the production of clavulanic acid from all of the microorganisms recited in claim 32. However, Puentes et al disclose that all of the claimed microorganisms were known at the time of applicant's invention to produce clavulanic acid in known media containing carbon sources, nitrogen sources and inorganic salts. See page 2. Thus, the substitution of any known clavulanic acid-producing species for that disclosed in Cole and Lawrence clearly would have been considered an obvious matter of selecting from known equivalents, the artisan of ordinary skill

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reasonably expecting from Puentes that the microorganisms disclosed therein would be able to produce clavulanic acid in the fermentation media disclosed by Cole. Thus, absent some unexpected result inhering from the use of the claimed microorganisms, the claims must be considered obvious in this respect.

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
March 27, 2001